



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT

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AUG 01 2002

*In re* Application of )

Michael A. Innis *et al.* )

Serial No. 09/639,273 )

Filed: August 15, 2000 )

Examiner: Eliane Lazar-Wesley

Group Art Unit: 1646

Atty. Dkt. No. 012441.00002

TECH CENTER 1600/2900

For: **Production of Tissue Factor Pathway Inhibitor**

**SUBMISSION OF EXECUTED DECLARATION UNDER RULE 132**

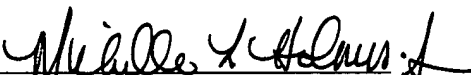
The Honorable Assistant Director of  
Patents  
Washington, D.C. 20231

Sir:

Applicants submitted an unexecuted Declaration of Dr. Abba Creasey under Rule 132 on July 29, 2002. Applicants submit herewith the signed and dated Declaration. No fee is believed due to make this submission filed timely. If any fees are due please charge our Deposit Account No. 19-0733.

Respectfully submitted,

Date: July 31, 2002

By:   
Michelle L. Holmes-Son  
Registration No. 47,660

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**For: Production of Tissue Factor Pathway Inhibitor****DECLARATION UNDER RULE 132**

I, Abba A. Creasey, hereby declare:

1. I am named as a joint inventor of the application referenced above.
2. I am an employee of Chiron Corporation, and all of the work described in the application was performed at Chiron Corporation.
3. In my experience, the activity of TFPI expressed in and purified from *Saccharomyces cerevisiae* as described in the above-identified application is similar to the activity of TFPI expressed in and purified from mammalian baby hamster kidney (BHK) cells.
4. Experiments conducted in our laboratories have demonstrated that the activity of TFPI expressed in and purified from *S. cerevisiae* as described in the application is also similar to the activity of TFPI expressed in and purified from *E. coli*.
5. The activity of TFPI expressed in and purified from *E. coli* is nearly identical to the activity of TFPI expressed in and purified from mammalian C127 cells. See Ho *et al.* (*Blood*, 95, 2000, 1973-1978; Exhibit 1), which teaches that TFPI expressed in and purified from mammalian C127 cells inhibits factor Xa activity similarly to TFPI expressed in and purified from *E. coli*. (See Fig. 2 and page 1975, column 2, lines 1-5.)
7. The TFPI expressed in and purified from *E. coli* used by Ho *et al.* was also used to determine that the *S. cerevisiae*-expressed and purified TFPI described in the application has activity that is similar to *E. coli*-expressed and purified TFPI. Ho *et al.* obtained the *E. coli*-

purified TFPI from Monsanto Company (Exhibit 1, page 1973, second column, lines 8-9, of the Materials and Methods.) Monsanto Company and Chiron corporation have a joint venture on the TFPI project, whereby Chiron manufactures *E.coli* expressed TFPI and provides purified TFPI to Monsanto and collaborators. 8. The activity of TFPI purified from C127 cells is similar to the activity of TFPI purified from BHK cells. See Wun *et al.* (*Thrombosis and Haemostasis*, 68, 1992, 54-59; Exhibit 2), which teaches that TFPI expressed in and purified from C127 cells has similar factor Xa inhibitory activity as TFPI expressed in and

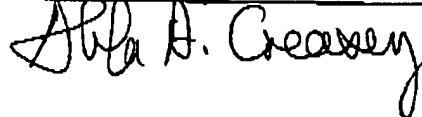
purified from BHK cells. (Page 56, column 2, lines 34-39.) See also Nordfang *et al.* (*Biochemistry*, 30, 1991, 10371-10376; Exhibit 3), which teaches that TFPI expressed in and purified from C127 cells has similar anticoagulant activity in a PT coagulation time assay to TFPI expressed in and purified from BHK cells. (Page 10371, column 2, lines 12-20.) Valentin *et al.* (*Blood Coagulation and Fibrinolysis*, 2, 1991, 629-635; Exhibit 4) also teaches that TFPI expressed in and purified from C127 cells has similar anticoagulant activity in a clotting time assay to TFPI expressed in and purified from BHK cells.

12. The activities of TFPI expressed in and purified from *S. cerevisiae* as described in the application, TFPI expressed in and purified from *E. coli*, TFPI expressed in and purified from C127 cells, and TFPI expressed in and purified from BHK cells are all similar. Therefore, the activity of the TFPI that is expressed in and purified from *S. cerevisiae* as described in the application is similar to the activity of TFPI expressed in and purified from BHK cells.

13. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these were made with the knowledge that false statements made willfully are punishable by fine, imprisonment, or both a fine and imprisonment under Section 1001 of Title 18 of the United States; and further that false statements made willfully may jeopardize the validity of any patent issuing on an application in which the false statements were made.

Date 7/25/02

Abla A. Creasey



Please type a plus sign (+) inside this box → ☐

PTO/SB/21 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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# TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number 09/639,273

Filing Date August 15, 2000

First Named Inventor Michael A. Innis et al

Group Art Unit 1646

Examiner Name Eliane Lazar-Wesley

Total Number of Pages in This Submission

Attorney Docket Number 012441.00002

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## ENCLOSURES (check all that apply)

☐ Fee Transmittal Form

☐ Fee Attached

☐ Amendment / Response

☐ After Final

☒ Declaration Under  
Rule 132 (Executed)

☐ Extension of Time Request

☐ Express Abandonment Request

☐ Information Disclosure Statement

☐ Certified Copy of Priority  
Document(s)

☐ Response to Missing Parts/  
Incomplete Application

☐ Response to Missing  
Parts under 37 CFR  
1.52 or 1.53

☐ Assignment Papers  
(for an Application)

☐ Drawing(s)

☐ Licensing-related Papers

☐ Petition

☐ Petition to Convert to a  
Provisional Application

☐ Power of Attorney, Revocation  
Change of Correspondence Address

☐ Terminal Disclaimer

☐ Request for Refund

☐ CD, Number of CD(s) \_\_\_\_\_

☐ After Allowance Communication to  
Group

☐ Appeal Communication to Board of  
Appeals and Interferences

☐ Appeal Communication to Group  
(Appeal Notice, Brief, Reply Brief)

☐ Proprietary Information

☐ Status Letter

☒ Other Enclosure(s)  
(please identify below):

**Submission of Executed  
Declaration Under Rule 132**

Remarks

## SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm  
or  
Individual name

Michelle L. Holmes-Son, Reg. No. 47,660

Signature

*Michelle L. Holmes-Son*

Date

July 31, 2002

## CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on this date: \_\_\_\_\_

Typed or printed name

Signature

Date

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.